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THE PRISONER'S DILEMMA: THE HISTORY,
ETHICAL DIMENSIONS, AND EVOLVING REGULATORY
LANDSCAPE OF CLINICAL TRIALS ON INMATES

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ABSTRACT

The history of research on prisoners in the United States is marred with a shameful past of abuse and coercion. With the development of research ethics arising from the Nuremberg Code and the Belmont Report, a critical light was shone on these oppressive practices. In 1974, the Department of Health and Human Services commissioned a group to investigate the conditions under which prisoners were used as research subjects and to formulate recommendations to guide clinicians in the future. The results of this Commission Report paved the way for Subpart C of the HHS regulations, which classifies prisoners as a vulnerable population and created a de facto ban on the use of inmates in any research study that received federal funding. What made this situation particularly noteworthy was the position of the FDA following this eventful change in regulation. Initially, the FDA proposed a rule similar to that of HHS which would have effectively barred the use of prisoners in all clinical research on FDA-regulated products, even that which was privately funded. This proposal was met with staunch resistance, and a lawsuit filed by prisoners and a pharmaceutical company claimed that their constitutional rights would be violated by this de facto ban. The FDA eventually settled the case, and never again revisited the issue. But recently, the question of the propriety of using prisoners in clinical trials has once again entered the public consciousness. The vast discrepancy in approaches to this sensitive issue by the two major bodies tasked with its regulation yields fruitful insight into the moral and ethical implications of research on prisoners. Strong advocates on both sides of the issue insist that respect for persons, beneficence, and justice all weigh heavily in their favor. These issues come most starkly into relief when viewed through an Eighth Amendment paradigm of “cruel and unusual punishment,” as well as a Fourteenth Amendment analysis under a “due process” and “equal protection” framework. The timeliness of this issue is apparent given the recent developments in this area of bioethics which has been relatively dormant for decades. A report by the Institute of Medicine in 2006, followed by an Advance Notice of Proposed Rulemaking from the HHS in 2011, indicates that change is afoot. Now is the critical moment to appraise the situation and strike the appropriate balance between protecting prisoners from abuse, universalizing the regulatory landscape to promote medical progress, and ensuring that the constitutional rights of prisoners as a class are defended.

TABLE OF CONTENTS

Introduction.....	1
I. Development of the Doctrine of Informed Consent	2
II. History of Research on Prisoners	6
III. The Ethics of the Debate.....	9
A. Arguments Against Research on Prisoners	9
1. Inability to Give Sufficiently Free and Informed Consent	9
2. Motivations for Prisoners to Participate in Medical Experiments	10
B. Arguments For Research on Prisoners	15
1. A Special Moral Privilege.....	16
2. Eighth Amendment Claims.....	16
3. Fourteenth Amendment Claims	20
4. Controlled and Diverse Population.....	21
IV. Current Regulation of Human Subject Research.....	21
A. HHS Regulation of Research on Prisoners	23
B. FDA Regulation of Research on Prisoners	26
V. Recent Developments	29
A. 2006 IOM Report	29
B. 2011 Notice of Proposed Rulemaking	31
VI. Proposals for Regulatory Reform	33
Conclusion	37

INTRODUCTION

The development and progress of medical science relies on a process of trial and error through which innovative therapies and groundbreaking techniques are proven safe and effective. This method requires experimentation on those willing to contribute their bodies to the advancement of medicine. Every new lifesaving breakthrough begins with one human subject, the first person to give himself to the clinical trial with the hope and trust that he will come out alive. Without these volunteers, drug development as it operates today could not exist. But a question arises when we think about these brave human subjects who risk everything to contribute to medical progress—what motivates them and do they know what could happen if a drug is actually unsafe and ineffective? A litany of atrocities over the course of human history have led to a set of norms about the permissible risks we allow people to take and a basic level of understanding and voluntariness they must possess before they are allowed to participate. It is in reference to certain populations that these questions come to the fore: the destitute, the disabled or mentally-ill, children and the elderly, pregnant women, and prisoners. The regulation of research on prisoners in the United States is particularly note-worthy given that there is no clear consensus of the “right answer,” even among the federal bodies tasked with making the decision.

In this paper, I will examine why there exists a discrepancy between the Department of Health and Human Services (HHS) regulations of research on prisoners and those of the Food and Drug Administration (FDA). I will also explore whether the current regulatory regime should be adjusted to reflect the changing landscape of drug development and experimentation. In Part I, I will discuss the development of the doctrine of informed consent and the primary historical events in the timeline of human subject research that led to the promulgation of the Belmont Report. Part II will address the history of research on prisoners in the United States

prior to the develop of codes of research ethics, demonstrating how and why this debate arose and what led many to fear the use of prisoners in medical experimentation. Part III will flesh out the ethics of the debate and the arguments for and against using inmates as research subjects. In Part IV, I will sketch the current regulatory landscape of prisoner research, explaining the parallel jurisdiction of HHS and the FDA. I will describe the impetus for HHS' total ban on prisoner subject research, as well as the FDA's initial move towards a ban but subsequent removal of most restrictions on private pharmaceutical companies' experimentation on prison populations. Part V will address recent developments in this area and the push towards the relaxing of HHS' total ban. Finally, in Part VI, I will propose potential areas of regulatory reform, with suggestions for future development in line with contextual changes in the decades since these regulations were enacted.

I. DEVELOPMENT OF THE DOCTRINE OF INFORMED CONSENT

The defendants in this case are charged with murder, tortures and other atrocities committed in the name of medical science. The victims of those crimes are numbered in the hundreds of thousands. A handful are still alive; a few of the survivors will appear in this courtroom. But most of these miserable victims were slaughtered outright or died in the course of the tortures to which they were subjected.

For the most part they are nameless dead. To their murderers, these wretched people were not individuals at all. They came in wholesale lots and were treated worse than animals.¹

With this powerful condemnation, the chief counsel for the prosecution, Brigadier General Telford Taylor, delivered the opening statement at the Nuremberg Tribunal.² So began the

¹ GEORGE J. ANNAS & MICHAEL A GRODIN, *THE NAZI DOCTORS AND THE NUREMBERG CODE: HUMAN RIGHTS IN HUMAN EXPERIMENTATION* 6 (1992).

² *See id.*

criminal proceedings against twenty-three leading German physicians for the gruesome atrocities committed against concentration camp prisoners under the guise of medical experimentation.³

The shocking accounts elicited from the Tribunal reverberated around the world, shaking into the public consciousness the potentially disastrous consequences of medical research on unwilling subjects.⁴ In response, in 1946 a group of doctors and lawyers “promulgated a code of behavior to guide medical research torn by sometimes conflicting desires to conquer disease and at the same time to respect the integrity of the individual patient.”⁵ Thus was born the Nuremberg Code—the first international document to espouse the necessity of informed consent and voluntary participation in experimental research.⁶ Though not binding on any individual or nation state, the Code laid the groundwork for an international set of norms regulating research

³ See Trials of War Criminals Before the Nuremberg Military Tribunal Under Control Council Law No. 10, *United States of America v. Karl Brandt et al.* (1948).

⁴ See Colleen M. McCarthy, Note, *Experimentation of Prisoners: The Inadequacy of Voluntary Consent*, 15 NEW ENG. J. ON CRIM. & CIV. CONFINEMENT 55, 57 (1989).

⁵ Marian F. Ratnoff & Justin C. Smith, *Human Laboratory Animals: Martyrs for Medicine*, 36 FORDHAM L. REV. 673, 673 (1968).

⁶ See K.C. Kalmbach & Phillip M. Lyons, *Ethical and Legal Standards for Research in Prisons*, 21 BEHAV. SCI. LAW 671, 674 (2003). The free and informed consent portion of the Nuremberg Code states:

1. The voluntary consent of the human subject is absolutely essential.
This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonable to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

in clinical trials.⁷ The Code required that the consent of the experimental subject exhibit four critical characteristics: the consent must be competent, voluntary, informed, and comprehending.⁸

In 1964, the World Medical Association released its own guidance document directed towards medical doctors conducting research on human subjects.⁹ This Declaration of Helsinki in many ways superseded the Nuremberg Code and became the governing document for international research ethics.¹⁰ Among other things, the Declaration established that research protocols should be reviewed by an independent committee prior to implementation, the risks of any trial should not exceed the predicted benefits, and that research subjects “must be adequately informed of the aims, methods, source of funding, any possible conflicts of interest, [and] institutional affiliations of the researcher.”¹¹

⁷ Udo Schüklenk, *Protecting the vulnerable: testing times for clinical research ethics*, 51 SOC. SCI. & MEDICINE 969, 972 (2000). Commentators have remarked on the peculiarity of establishing “norms” which in fact must be strictly enforced and policed:

The use of human subjects in behavioral and biomedical research is today circumscribed by a quite elaborate set of rules, regulations, and guidelines. These legal and ethical strictures give force to what are perceived as certain fundamental moral principles guiding man’s treatment of his fellow man. The source of these principles is variously traced to ‘natural law,’ man’s ‘humanity,’ or some other hopeful metaphysical construct whose observance would be considered, or so the aspiration is, a matter of course for all civilized societies. However, the articulation of these principles as in any way binding, as law, has generally come in the aftermath of historical experience that directly contradicts the benign assumption that they are universally shared or adhered to.

Kalmbach & Lyons, *supra* note 6, at 672.

⁸ GEORGE J. ANNAS, INFORMED CONSENT TO HUMAN EXPERIMENTATION: THE SUBJECT’S DILEMMA 7 (1977).

⁹ See Kalmbach & Lyons, *supra* note 6, at 675.

¹⁰ See Schüklenk, *supra* note 7, at 972.

¹¹ Kalmbach & Lyons, *supra* note 6, at 676.

The national conscience was again rocked in the early 1970s when it was discovered that the U.S. Public Health Service had been conducting the Tuskegee Syphilis Study for forty years, flagrantly violating the principles of autonomy and informed consent of research subjects.¹² The study involved approximately 400 African-American males who were infected with syphilis and denied treatment in order to study the progression of the disease.¹³ Even after penicillin became available in the 1950s, the men were prevented from seeking treatment, were lied to and told that they were already being treated, and often died without appropriate medical intervention.¹⁴ The study came to light in 1973, and in the face of national outrage, was finally put to an end by the U.S. Department of Health, Education, and Welfare.¹⁵ In response, the National Research Act of 1974 was passed.¹⁶ This legislation created the National Commission for the Protection of Human Subject of Biomedical and Behavioral Research, which was tasked with identifying the basic ethical principles to be protected in clinical research and constructing guidelines for future researchers with those principles in mind.¹⁷ The Belmont Report was issued in 1979, elucidating the three fundamental ethical principles underlying human subject research and demonstrating how these principles should be applied in research protocols.¹⁸ These principles—respect for persons, beneficence, and justice—laid the ethical foundation which continues to undergird

¹² See *id.* at 673.

¹³ See *id.* The men were drawn to the study through advertisements of “special free treatment” and were not told that they had in fact received placebos known to be ineffective. See Allen M. Brandt, *Racism, Research and the Tuskegee Syphilis Study*, 8 THE HASTINGS CENTER REPORT 21 (1978).

¹⁴ See Kalmbach & Lyons, *supra* note 6, at 673.

¹⁵ See *id.*

¹⁶ See *id.* at 676.

¹⁷ See *id.*

¹⁸ Alison Wichman, *Protecting Vulnerable Research Subjects: Practical Realities of Institutional Review Board Review and Approval*, 1 J. HEALTH CARE L. & POL’Y 88, 89 (1998).

current law governing research on humans.¹⁹ “Respect for persons” highlights the autonomy and dignity of human beings and requires that subjects give informed consent in order to participate in research studies.²⁰ “Beneficence” ensures that the harms of research are minimized while the benefits are maximized, which requires a risk/benefit analysis of the research protocol *ex ante* by an institutional review board.²¹ Finally, the principle of “justice” speaks to the selection of research subjects to ensure that certain classes of individuals are not “systematically selected for or excluded from research, unless there are scientifically or ethically valid reasons for doing so.”²²

II. HISTORY OF RESEARCH ON PRISONERS

What happened at Holmesburg was just as gruesome as Tuskegee, but at Holmesburg it happened smack dab in the middle of a major city, not in some backwoods in Alabama. It just goes to show how prisons are truly distinct institutions where the walls don’t just serve to keep inmates in, they also serve to keep public eyes out.²³

These words of Allen M. Hornblum, the author of “Acres of Skin,” exemplify the view of many looking back on the history of research on prisoners in the United States. The stories of atrocities inflicted on inmates prior to the promulgation of the Belmont Report are striking. The earliest known experimentation on prisoners in the United States began in 1914, when twelve Mississippi inmates were infected with pellagra, a disease which causes diarrhea, dermatitis, dementia, and possibly death.²⁴ The experiment involved the inducement of the disease in order

¹⁹ *Id.*

²⁰ *Id.*

²¹ *Id.* at 90.

²² *Id.*

²³ Ian Urbina, *Panel Suggests Using Inmates in Drug Trials*, NEW YORK TIMES, Aug 13, 2006.

²⁴ Sharona Hoffman, *Beneficial and Unusual Punishment: An Argument in Support of Prisoner Participation in Clinical Trials*, 33 IND. L. REV. 475, 482 (2000).

to study the effect of diet on its progression; despite begging to be released from the trial after suffering severe symptoms, the prisoners were forced to continue the experiment.²⁵ Testicular transplant experiments were conducted on five hundred prisoners at San Quentin, California to test whether lost male potency could be reinvigorated.²⁶ In the 1940s, in an attempt to develop new drugs to treat malaria during World War II, Chicago-area doctors infected four hundred prisoners with the disease—these studies would later be cited by Nazi doctors in the Nuremberg trials as precedent to defend their own research supposedly conducted to aid the German war effort.²⁷

The list goes on: in 1942, Harvard biochemist Edward Cohn injected sixty-four Massachusetts prisoners with beef blood in a U.S. Navy-funded experiment; in 1950, Dr. Joseph Stokes of the University of Pennsylvania infected two-hundred female prisoners with viral hepatitis; and from 1951-1960, the University of Pennsylvania, under contract with the United States Army, conducted psychopharmacological experiments on hundreds of prisoners. In the early 1950s, nearly all participants in Phase I clinical trials across the country were prisoners, subject to experiments studying hepatitis, heart disease, and intestinal protozoan parasites, among other ailments.²⁸ During this period, inmates in the Ohio prison system were also injected with live cancer cells in both forearms in a study conducted by the Sloan Kettering Institute for

²⁵ *See id.*

²⁶ *See id.*

²⁷ *See id.*; see also Vera Hassner Sharav, *Human Experiments: A Chronology of Human Research*, ALLIANCE FOR HUMAN RESEARCH PROTECTION, available at <http://www.ahrp.org/history/chronology.php>.

²⁸ *See Hoffman, supra* note 24, at 485.

Cancer Research and Ohio State University.²⁹ Two weeks after the injection, the area of malignant cells was removed from one arm, but remained in the other arm indefinitely.³⁰

From 1963 to 1973, the Atomic Energy Commission conducted testicular irradiation experiments on prisoners in Oregon and Washington to determine how much radiation astronauts could tolerate during space flights.³¹ The researchers paid the prisoners \$5 a month to undergo extensive radiation exposure to their testicles, and ultimately paid them \$100 at the end of the trial when they received a vasectomy.³² At Holmesburg Prison, between 1952 and 1974, University of Pennsylvania dermatologist Dr. Albert Kligman conducted experiments of skin products on prisoners by the hundreds.³³ He tested radioactive isotopes on the prisoners, despite having little education about radioactive medicine.³⁴ Within this same time period, thirty-three pharmaceutical companies tested 153 experimental drugs on the Holmesburg prisoners.³⁵ From 1965-1966, Dow Chemical used these prisoners for dioxin experiments, a component of Agent Orange.³⁶ It is reported that Kligman exposed prisoners to 7500 micrograms of the highly toxic substance, 486 times the dosage he was advised to administer by Dow Chemical.³⁷ Upon his first visit to the prison in 1966, Dr. Kligman famously stated, “All I saw before me were acres of skin.”³⁸ In a similar vein of objectification, a researcher in 1973 was quoted as remarking in

²⁹ *See id.*

³⁰ *See id.*

³¹ *See id.* at 486.

³² Sharav, *supra* note 27.

³³ *See id.*

³⁴ *See Hoffman, supra* note 24, at 487.

³⁵ *See id.* *See also* Urbina, *supra* note 23.

³⁶ *See Hoffman, supra* note 24, at 487.

³⁷ *Id.*

³⁸ ALLEN M. HORNBLUM, ACRES OF SKIN: HUMAN EXPERIMENTS AT HOLMESBURG PRISON xx (1998).

confidence that prisoners are “. . . fine experimental material . . . and much cheaper than chimpanzees.”³⁹

III. THE ETHICS OF THE DEBATE

The ethical implications of clinical research on prisoners are brought most starkly into relief when considering the principle of “respect for persons.” On the one hand, respect for prisoners as autonomous agents capable of rational decision-making seems to require that prisoners not be deprived of the opportunity to volunteer in clinical research studies.⁴⁰

Alternatively, the particularities of incarceration may present unavoidable coercion or undue influence, such that respect for prisoners may warrant barring them from participation in research to ensure that they do not subject themselves to greater risk that they would if not incarcerated. It is ultimately these competing visions of “true” respect which animate the debate over the moral and ethical permissibility of clinical research on prisoners.

A. Arguments Against Research on Prisoners

1. Inability to Give Sufficiently Free and Informed Consent

One of the strongest statements against research on prisoners comes from Patricia King, a member of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. In her resounding refutation of the possibility of a prisoner’s informed consent to nontherapeutic research, she argued that prisons are total institutions which, by their inherent character and purpose, make sufficiently free consent to research unattainable: “I,

³⁹ Gregory Dober, *Cheaper Than Chimpanzees: Expanding the Use of Prisoners in Medical Experiments*, 19 PRISON LEGAL NEWS 1, 1 (2008).

⁴⁰ See Rachel Wener, *Not Situated to Exercise Free Power of Choice: Human Subject Research in Prison Settings*, 26 TEMP. J. SCI. TECH. & ENVTL. L. 365, 369 (2007).

personally, do not believe that theoretically one can ever remove enough of the constraints from a prison to afford self-determination because by the time you removed them all you would not have a prison.”⁴¹ Others have similarly argued that the experience of incarceration engenders motivations in prisoners which induce them to participate in experiments under conditions to which they would not consent if free.⁴² The inability to disambiguate those prisoners who are capable of giving sufficiently free consent from those who are not also animates the discussion.⁴³ As espoused by a federal court in Maryland, the two critical elements necessary to establish informed consent under American law are information and voluntariness.⁴⁴ In this context, “voluntariness” means the following: “[t]he person consenting must be ‘so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion.’”⁴⁵ It is argued that subtle forms of coercion in the prison context act to undermine freedom of choice and deprive a prisoner of the right to be “master of his own body.”⁴⁶

2. Motivations for Prisoners to Participate in Medical Experiments

The most commonly cited incentives for prisoners to volunteer for nontherapeutic research include: the ability to obtain financial compensation, hope for a reduction of sentence or greater likelihood of being released on parole, seeking of psychiatric or medical help, relief from the tedium of prison existence, desire for better living conditions, attraction of risk-taking, and

⁴¹ Roy Branson, *National Commission Says ‘No, Unless...,’* THE HASTINGS CENTER REPORT 15, 17 (1977).

⁴² See, e.g., Colleen M. McCarthy, *Experimentation on Prisoners: The Inadequacy of Voluntary Consent*, Note, 15 NEW ENG. J. ON CRIM. & CIV. CONFINEMENT 55, 60 (1989).

⁴³ See Branson, *supra* note 41, at 17.

⁴⁴ *Baily v. Lally*, 481 F. Supp. 203, 220 (D. Md. 1979).

⁴⁵ McCarthy, *supra* note 42, at 61.

⁴⁶ Marian F. Ratnoff & Justin C. Smith, *Human Laboratory Animals: Martyrs for Medicine*, 36 FORDHAM L. REV. 673, 684 (1968).

altruism.⁴⁷ From a legal perspective, the conditions that give rise to these motivations may constitute duress such as would render a contract voidable and, analogously, undercut a prisoner's "informed consent" to participation in research.⁴⁸

In regard to the motivation of financial reward, the primary question to determine coercion is whether there are alternative sources of equal income and whether consenting to participate in research is the only way prisoners can earn enough money to sustain a minimum standard of living.⁴⁹ The amount of money paid for participation in drug trials vis-à-vis wages for other types of prison work is particularly salient. One study notes:

[T]he amount of pay offered to prisoners to participate in drug trials may be three to fifteen times as great as the rate of pay for other jobs available in the prison. . . . [T]his constitutes an undue inducement to participate in research. At the same time, the amount of money drug firms pay to prisoner volunteers is approximately one-tenth that customarily paid to free-living volunteers [T]his constitutes an incentive to drug companies to do most of their drug testing on prisoners.⁵⁰

A related motivation to participate in drug trials is the difference in environment between the normal prison wards and the area which houses research subjects. A specific example from the Maryland House of Corrections illuminates this potentially coercive element.⁵¹ The facts of *Bailey v. Mandel*⁵² describe a prison filled with 1640 inmates, 700 more than its maximum capacity, and ceaseless noise, violence, and homosexual attacks.⁵³ The prisoners were required to purchase all health and hygiene products from the commissary, including soap, toothpaste,

⁴⁷ See NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH, REPORT AND RECOMMENDATIONS: RESEARCH INVOLVING PRISONERS 61, U.S. Department of Health, Education, and Welfare, DHEW Pub. No. (OS) 76-131 (1976) [hereinafter REPORT AND RECOMMENDATIONS].

⁴⁸ *Id.*

⁴⁹ *Id.* at 62.

⁵⁰ McCarthy, *supra* note 42, at 62.

⁵¹ See ANNAS, *supra* note 8, at 113.

⁵² Md. District Ct., K-74-1102 (filed Oct. 8, 1974).

⁵³ ANNAS, *supra* note 8, at 113.

razor blades, and deodorant, which were sold at a cost equal to or greater than that in a grocery store.⁵⁴ The estimated cost of these items was \$11 every two weeks, yet the average pay for most prison jobs was \$0.65 per day.⁵⁵ Thus, the prisoners could not afford to maintain even a minimum standard of personal hygiene. In comparison, the Infectious Disease Area which housed participants in research studies was spacious, well-lit, air-conditioned, had a color television and a kitchen stocked with food.⁵⁶ The subjects were given comfortable beds and permitted to take frequent private showers.⁵⁷ The compensation for research subjects was \$10 per day.⁵⁸ The coercion inherent in this situation is the fact that participation in the research experiment was the only way prisoners could achieve a minimum standard of living.⁵⁹ Thus, their willingness to be exposed to typhoid, dysentery, malaria, Rocky Mountain spotted fever, influenza, and cholera were unduly influenced by the horrendous living conditions they would remain in if they refused to participate.⁶⁰

Other prisoners cite fear as a motivating factor in the participation in medical research and consequent removal from the typical prison setting. Being placed in the separate research unit allowed prisoners to sleep “without being afraid someone [will] ‘bust them in the head’ or

⁵⁴ *Id.*

⁵⁵ *Id.*

⁵⁶ *Id.*

⁵⁷ *Id.*

⁵⁸ *Id.*

⁵⁹ *See id.* at 114. In the words of one professor of law and ethics, “When the ‘reward’ is such as only to give us the necessary conditions of [basic] rights and freedoms—when all that the reward does is to bring us up to a level of living to which we are entitled, and of which we have been deprived by man—then the ‘reward,’ I think, constitutes duress. A reward which accrues to one who has achieved this level, or who can easily achieve it ... and which hence serves only to grant us ‘luxury’ items, does not constitute duress, and hence does not render choice unfree, no matter how great this reward may be.” *Id.* at 114-15.

⁶⁰ *See id.* at 113.

‘set fire’ to their bunks while they [sleep].”⁶¹ Similarly, in Statesville Prison in Illinois, where an antimalarial drug research experiment was conducted in 1974, fear of attack was so pervasive throughout the prisoner community that almost forty men requested relocation to solitary confinement for their own safety.⁶²

The motivation of reprieve from the monotony and boredom of prison life also may play a role in a prisoner’s decision to volunteer in a research study. As an example, prisoners in the Maryland House of Correction without jobs spend sixteen to seventeen hours per day alone in their cells.⁶³ Escape from this tedious existence at any cost may constitute undue influence on the choices of prisoners.

The “parole incentive” is another hugely influential factor in a prisoner’s decision-making, and one which must be examined carefully and policed heavily. Well into the 1950s, it was common for prisoners to be rewarded for participation in medical research by early parol or the commutation of one’s sentence.⁶⁴ In 1948, the Governor of Illinois formed a committee to examine the practice of paroling prisoners who volunteered as subjects in malaria research.⁶⁵ The Green Committee, as it was called, determined that although “a reduction of sentence in prison . . . can amount to undue influence,” the parole system was meant to reward “good conduct and industry” and “exceptional bravery or fidelity in a good cause.”⁶⁶ As such, the practice of paroling research volunteers was deemed permissible.⁶⁷ To this day, the hope that a parole board will view a prisoner’s contribution to medical progress favorably may continue to

⁶¹ McCarthy, *supra* note 42, at 64.

⁶² ANNAS, *supra* note 8, at 115.

⁶³ *Bailey*, 481 F. Supp. at 205.

⁶⁴ *See* McCarthy, *supra* note 42, at 63.

⁶⁵ *See* ANNAS, *supra* note 8, at 116.

⁶⁶ *Id.*

⁶⁷ *See id.*

animate decisions of consent. In the *Bailey* case, for example, the doctors conducting the research would write a letter to the parole board informing them of the inmate's participation in the study.⁶⁸ Whether or not this practice was permitted to play any role in the parole board's decision making process, it nonetheless may have unduly influenced a prisoner to volunteer on the off chance of a possible benefit in parole.⁶⁹ A 1975 case filed in Connecticut alleged that two of the three prisoner-plaintiffs had been denied parole and were told that their denials were due to their lack of participation in a research study.⁷⁰ At this time, Connecticut's public policy explicitly denounced the practice of considering prisoner participation in experiments in regard to parole decisions.⁷¹ However, after this case was filed, the correctional facility soon settled with the plaintiffs, the prisoners were given new parole hearings in front of a board which was unfamiliar with the research study, and all three were granted parole.⁷² According to American jurisprudence, the threat of imprisonment satisfies the legal definition of duress.⁷³ Thus, the promise of release from prison or a reduction in sentence as a reward for participation in an

⁶⁸ See McCarthy, *supra* note 42, at 63.

⁶⁹ See *id.*; see also *Bailey*, 481 F. Supp. at 221.

⁷⁰ See ANNAS, *supra* note 8, at 116; see also *Taylor v. Manson, et al.*, U.S.D.C. Conn., #H-75-37 (filed Jan. 29 1975). The study which the prisoners were coerced to join was a behavioral modification program for pedophiles which utilized faradic aversive conditioning and covert sensitization. The faradic aversive conditioning portion involved placing electrodes on the upper thighs of the prisoner and showing him slides of adults and children. When a slide of a child was shown, the prisoner received a painful electric shock if he did not ask for the slide to be changed within three seconds. The covert sensitization portion involved taping an interview with the prisoner describing his pedophilic fantasies, and then hypnotizing the prisoner and replaying portions of the tape paired with suggestions of frightening and painful events such as being attacked by rats, suffocating, or being castrated with a hot iron. These sessions were conducted twenty times for sixty to seventy minutes each. ANNAS, *supra* note 8, at 117.

⁷¹ See *id.*

⁷² See *id.*

⁷³ ANNAS, *supra* note 8, at 115.

experiment is inherently coercive, for the implicit assertion is that refusal to participate will result in the continuation of imprisonment.⁷⁴

B. Arguments For Research on Prisoners

As discussed herein, the question of coercion and voluntariness is a primary concern in conducting research on prisoners. However, even in the Commission Report which led to the HHS ban on research on inmates, the data was conflicted and this issue was far from clear. At that time, a group of sociologists presented the Commission with data indicating that prisoners were in fact able to voluntarily consent.⁷⁵ Three types of prisoner profiles emerged from their study, each of which rejected the notion that prisons as an institution implicitly hinder freedom of choice.⁷⁶ The first profile was a prisoner who identified strongly with prison life and would likely refuse to participate in research given that this activity would seem too cooperative with the prison regime. The second profile was prisoners who identify with social norms and would like to volunteer for research out of altruism. The third model was an independent actor who would conduct an internal cost-benefit calculus and choose to participate when it would maximize their comfort level without too great a risk.⁷⁷ The conclusion of these sociologists was opposed to banning research in prisons; rather they argued that prisoner research should be allowed but that an oversight board should ensure that the subjects were fully informed of the risks and benefits of the research.⁷⁸

⁷⁴ *Id.*

⁷⁵ Appendix to REPORT AND RECOMMENDATIONS, *supra* note 47, at 4-1, 4-8 to 4-18.

⁷⁶ See Kathleen Schroeder, *A Recommendation to the FDA Concerning Drug Research on Prisoners*, 56 S. CAL. L. REV. 969, 977 (1982).

⁷⁷ *Id.*

⁷⁸ *Id.*

1. A Special Moral Privilege

The history of prisoner research, despite the instances of coercion and abuse, also provides an interesting example of the salutary aspects of allowing inmates to volunteer as research subjects. During World War II, as a means of demonstrating their patriotism and contributing to the war effort, prisoners would volunteer to test drugs needed by soldiers.⁷⁹ For example, prisoners would test the effectiveness of synthetic anti-malarial drugs in response to quinine shortages caused by the war.⁸⁰ This self-sacrifice in the name of the war was viewed by both prisoners and the American populace at large as a “special moral privilege,” and at one point the American Medical Association even considered barring from participation those prisoners who had committed particularly heinous crimes.⁸¹

2. Eighth Amendment Claims

There is also a constitutional aspect to the denial of allowing prisoners as a population to participate in medical research studies. Prohibiting “seriously ill prisoners from participating voluntarily in clinical research may constitute [a] . . . contravention of their constitutional rights under the Eight Amendment and the Due Process and Equal Protection clauses.”⁸² Inmates suffering from hepatitis, HIV, and tuberculosis may be deprived of life-saving therapies if unable to participate in research on potential cures for those diseases.⁸³ The Eighth Amendment of the Constitution prohibits the infliction of “cruel and unusual punishment.”⁸⁴ While the language of

⁷⁹ See McCarthy, *supra* note 42, at 58.

⁸⁰ *Id.* at 58 n. 13.

⁸¹ *Id.* at 58 n. 14.

⁸² See Hoffman, *supra* note 24, at 476-77.

⁸³ *Id.* at 477.

⁸⁴ U.S.CONST. amend. VIII. The text ensures that “[e]xcessive bail shall not be required, nor excessive fines imposed, nor cruel and unusual punishment inflicted.” *Id.*

the Amendment was originally narrowly interpreted, later Supreme Court cases expanded the definition of “cruel and unusual punishment” to encompass “broad and idealistic concepts of dignity, civilized standards, humanity, and decency.”⁸⁵ This conception includes the medical treatment an inmate does or does not receive while incarcerated.⁸⁶ To prevail on an allegation of an Eighth Amendment violation, a plaintiff must “establish a grave deprivation of rights to which prison officials have reacted with deliberate indifference.”⁸⁷ A successful deliberate indifference claim based on improper medical treatment in prison must show that “prison officials (1) were aware of the individual’s serious medical need; and (2) disregarded, ignored, or refused to provide the inmate with treatment for that need.”⁸⁸ If the alleged Eighth Amendment violation stems from a prison policy rather than the acts of a particular prison official, the regulation is considered valid if it is “reasonably related to legitimate penological interests”⁸⁹ The four factor test to assess the reasonableness of the regulation states:

(1) ‘there must be a “valid, rational connection” between the prison regulation and the legitimate governmental interest put forward to justify it;’ (2) the court should determine whether there are alternative means of exercising the constitutional right that remains open to the inmates; (3) the court is to consider the impact that accommodation of the asserted constitutional right will have on guards, other inmates, and on the allocation of prison resources; and (4) the court should assess whether there are ready alternatives to the prison regulation – the absence of such ready alternatives suggests that the regulation is reasonable while their existence may be evidence of the opposite.’⁹⁰

⁸⁵ Hoffman, *supra* note 24, at 493 (citing Jackson v. Bishop, 404 F.2d 571, 579 (8th Cir. 1968)).

⁸⁶ *Id.* at 493 (citing Helling v. McKinney, 509 U.S. 25, 31 (1993)).

⁸⁷ *Id.* (citing Estelle v. Gamble, 429 U.S. 97, 106 (1976)).

⁸⁸ *Id.* at 494 (citing Farmer v. Brennan, 511 U.S. 825, 835 (1994)).

⁸⁹ *Id.* (citing Turner v. Safley, 482 U.S. 78, 89 (1987)).

⁹⁰ *Id.* (citing Walker v. Sumner, 917 F.2d 382,385 (9th Cir. 1990)).

The Eighth Amendment claims can cut both ways in regards to drug research on prisoners. In one context, as seen in the case of *Bailey v. Lally*,⁹¹ prisoners filed a class action under 42 U.S.C. § 1983 alleging that they had been coerced to participate in clinical investigations and therefore had been subject to cruel and unusual punishment.⁹² However, the alternative perspective views the deprivation of life-saving, cutting edge medical treatments from an entire class of persons as unconstitutional punishment which violates the Eighth Amendment. Desperately ill patients in prison may see clinical trials as the last chance to receive potentially-effective treatment given their highly circumscribed ability to access high-cost and quality health care while incarcerated.⁹³ An illustrative example of this situation is the disproportionately high rates of HIV infection among the incarcerated. A 1992 study found that while the incidence rate of HIV in the general population was 18 out of 100,000, the rate among prisoners was approximately 362 per 100,000.⁹⁴ AIDS is the leading killer in correctional facilities, accounting for up to two-thirds of all inmate deaths in certain states.⁹⁵ While current AIDS treatments ameliorate some of the symptoms of the disease, participation in clinical trials could offer prisoners otherwise-unattainable access to cutting-edge drugs and experimental techniques.⁹⁶ Although no court as of yet has rendered a decision on this issue, “[r]egulations prohibiting seriously ill prisoners from participation in clinical trials in all cases, including those in which their exclusion results in the denial of potentially life-saving therapy, are vulnerable to

⁹¹ 481 F. Supp. 203 (D. Md. 1979).

⁹² *Id.*

⁹³ See Hoffman, *supra* note 24, at 498.

⁹⁴ See James W. Marquart et al., *Health Condition and Prisoners: A Review of Research and Emerging Areas of Inquiry*, 77 THE PRISON JOURNAL 185 (1997).

⁹⁵ See Hoffman, *supra* note 24, at 498.

⁹⁶ See *id.*

constitutional attack.”⁹⁷ The jurisprudential foundation was laid in 1976 when the Supreme Court stated that the government is obligated to provide medical care for prisoners, and that “deliberate indifference to serious medical needs of prisoners constitutes the ‘unnecessary and wanton infliction of pain,’ proscribed by the Eighth Amendment.”⁹⁸ To prevail on a 42 U.S.C. § 1983 claim of a constitutional violation, a prisoner must show that the failure to allow her access to a clinical study is so grave as to violate “contemporary standards of decency.”⁹⁹ She must also prove that the prison officials have shown deliberate indifference to her medical condition and that her future health may be jeopardized as a result.¹⁰⁰

While the ability of a prisoner to successfully argue these elements of a § 1983 claim may appear dubious, it is telling to note that the Court in other prisoner-health related contexts has allowed complaints to go forward which focus on a potential health problem in the future. For example, in *Helling v. McKinney*,¹⁰¹ a prisoner alleged that he was suffering cruel and unusual punishment due to his placement in a cell with an inmate who smoked five packs of cigarettes a day, sold to him by the prison.¹⁰² This cell assignment, he argued, rendered him unable to escape the deleterious consequences of second-hand smoke inhalation.¹⁰³ After numerous appeals, the Supreme Court found that the complainant had stated a valid cause of action under the Eighth Amendment and would be permitted to put on evidence that society objectively considered the risk “to be so grave that it violates contemporary standards of decency to expose *anyone* unwillingly to such a risk” and that prison officials had shown deliberate indifference to the

⁹⁷ *Id.* at 499.

⁹⁸ *Id.* (citing *Estelle v. Gamble*, 429 U.S. 97, 103 (1976)).

⁹⁹ Hoffman, *supra* note 24, at 500.

¹⁰⁰ *See id.* at 500-01.

¹⁰¹ 509 U.S. 25 (1993).

¹⁰² *See id.* at 28.

¹⁰³ *See id.*

health hazards caused by this living arrangement.¹⁰⁴ While not directly analogous, the Supreme Court’s finding that this complaint was potentially meritorious on an Eighth Amendment violation makes it more likely that the deprivation of access to clinical trials may rise to the level of a constitutional violation.¹⁰⁵

3. Fourteenth Amendment Claims

The Due Process and Equal Protection Clauses of the Fourteenth Amendment may also mandate the inclusion of prisoners in clinical trials.¹⁰⁶ Prisoners may contend that a law or regulation which bars their participation in trials is “depriving them of the liberty to enjoy the benefits of clinical research or is endangering their lives if it is precluding access to potential life-saving treatment.”¹⁰⁷ Putative inmate-plaintiffs may also argue that their status as prisoners is an invalid basis on which to subject them to unequal treatment.¹⁰⁸ These arguments formed the basis of the claim in *Fante v. Department of Health and Human Services*,¹⁰⁹ which, as I will explain, led the FDA to halt the implementation of its proposed regulation barring research on prisoners in trials of FDA-regulated products.¹¹⁰

The state would likely argue that its reason for limiting research on prisoners is animated by its concern for the risk of coerced or involuntary consent. However, this compelling interest could likely be achieved through less restrictive means such as more stringent Institutional

¹⁰⁴ *Id.* at 36.

¹⁰⁵ *See Hoffman, supra* note 24, at 500.

¹⁰⁶ *See id.* at 504.

¹⁰⁷ *Id.* at 505.

¹⁰⁸ *See id.*

¹⁰⁹ No. 80-72778 (E.D. Mich. filed Oct. 10, 1980).

¹¹⁰ *See Hoffman, supra* note 24, at 505. As discussed *infra*, this case was eventually settled by the FDA placing a stay on the proposed regulation, so the claims were never adjudicated at trial.

Review Board (IRB) guidelines, uniform research protocol, and a focus on improving the other coercive elements of prison life.¹¹¹

4. Controlled and Diverse Population

Use of prisoners in nontherapeutic research became commonplace after WWII due to the highly controlled conditions available in a prison environment—ideal for isolating only those variables one intends to study.¹¹² The ability to control a subject’s diet, stimuli, environment, interactions with others, and a host of other factors is highly unique to an institutionalized setting such as a prison and may allow researchers to obtain more accurate results without unpredictable external influences. The diversity of the prison population may also aid the scientific validity of clinical research data. Traditionally, women, African-Americans, and Hispanics have all been underrepresented in clinical trials.¹¹³ A lack of gender and racial diversity in study populations adversely impacts the universality of the data and may harm future patients as well as the scientific community at large.¹¹⁴ Thus, the ability to incorporate these populations within a research subject pool would arguably improve both the lives of the prisoners and the results of the scientific study.

IV. CURRENT REGULATION OF HUMAN SUBJECT RESEARCH

While the Department of Health and Human Services (HHS) constitutes the umbrella federal agency sponsoring biomedical and behavioral research, its component parts include the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the Indian Health

¹¹¹ See Hoffman, *supra* note 24, at 506.

¹¹² McCarthy, *supra* note 42, at 58.

¹¹³ See Hoffman, *supra* note 24, at 509.

¹¹⁴ See *id.* at 510.

Service, and the Centers for Disease Control and Prevention (CDC).¹¹⁵ Regulatory jurisdiction over human experimentation in the United States has historically been split between the Food and Drug Administration and the Department of Health and Human Services.¹¹⁶ HHS issued regulations to govern research conducted or funded by government agencies, codified at 45 C.F.R. § 46.¹¹⁷ The FDA promulgated similar regulations dictating the required informed consent in research and clinical trials involving FDA-regulated products.¹¹⁸ These regulations, issued at 21 C.F.R. § 50 (protection of human subjects) and § 56 (Institutional Review Boards), present the minimum requirements of information given to clinical subjects, particularly the balance of risks and benefits.¹¹⁹ They also emphasize that no coercion may be applied to potential subjects in making their decision about whether or not to participate in the study.¹²⁰ In 1991, the core HHS regulations at 45 C.F.R. § 46, Subpart A were formally adopted by over a dozen other federal departments and agencies that conduct or fund human subject research and became the Federal Policy for the Protection of Human Subjects, or “Common Rule.”¹²¹ While this Federal Policy is now shared by seventeen departments and agencies, most privately-

¹¹⁵ See Wichman, *supra* note 18, at 90.

¹¹⁶ See Jennifer J. Couture, *Changes in Informed Consent in Experimental Procedures: The Evolution of a Concept*, 1 J. HEALTH & BIOMEDICAL L. 125, 134 (2004)

¹¹⁷ See Grant Bagley, *Informed Consent: The FDA’s Perspective*, 48 FOOD AND DRUG L.J. 181, 182 (1993).

¹¹⁸ See *id.* at 182.

¹¹⁹ *Id.*

¹²⁰ *Id.* at 183. This coercion element is particularly vital in an analysis of informed consent of prisoners. The regulations require that the investigator must minimize possible coercion or undue influence in eliciting consent, taking into account the timing, setting, identity of the person obtaining the consent, and other circumstances pertinent to the consent process and the potential subject’s ability to fully comprehend the risks and benefits of the study. *Id.* at 183-84.

¹²¹ COMMITTEE ON ETHICAL CONSIDERATIONS FOR REVISIONS TO DHHS REGULATIONS FOR PROTECTION OF PRISONERS INVOLVED IN RESEARCH, ETHICAL CONSIDERATIONS FOR RESEARCH INVOLVING PRISONERS 2 (2006) [hereinafter ETHICAL CONSIDERATIONS].

sponsored research is regulated by the FDA under 21 C.F.R. § 50 and § 56.¹²² Although the FDA regulations and the Common Rule are predominately parallel, a few significant differences exist.¹²³ One primary difference is the identification by HHS of certain classes of research subjects which require unique protections in research protocol.

A. HHS Regulation of Research on Prisoners

The HHS regulations specifically discuss “vulnerable populations,” reflecting the policy in the Belmont Report that the principle of “respect for persons” warrants additional protections for individuals with diminished autonomy.¹²⁴ Thus, the subpart concerning criteria for IRB approval of research stipulates a higher threshold of protection in research protocols where certain populations are involved: “When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.”¹²⁵

Subpart C of the Common Rule addresses in detail the restrictions on federally-funded research on prisoners. These restrictions, which have been in place since 1978, apply not only to research conducted by a federal agency or directly funded by federal capital, but also to private institutions which receive federal funding for any purpose, even if the research in question does not involve federal dollars.¹²⁶ The regulations forbid all biomedical or behavioral research on prisoners except studies particularly related to incarceration: the causes and effects of incarceration and criminal behavior, research on prisons as institutional structures, or the study

¹²² See *id.* at 6.

¹²³ See McCarthy, *supra* note 42, at 59.

¹²⁴ See Wichman, *supra* note 18, at 92.

¹²⁵ 45 C.F.R. § 46.111(b).

¹²⁶ See Wener, *supra* note 40, at 365, 371.

of conditions particularly affecting prisoners as a class.¹²⁷ As could be expected, this regulation significantly reduced the scope of research on prisoners to only those trials conducted by fully private, independent corporations.¹²⁸

Subpart C was enacted after the National Commission for the Protection of Human Subjects and Biomedical and Behavioral Research published its *Report and Recommendations: Research Involving Prisoners* in 1976.¹²⁹ Under the mandate set forth in section 202(a)(2) of the National Research Act, the Commission “studied the nature and extent of research involving prisoners, the conditions under which such research is conducted and the possible grounds for continuation, restriction or termination of such research.”¹³⁰ The Report detailed the state of research involving prisoners at the time, noting that both private pharmaceutical companies and governmental agencies use prisoners as subjects.¹³¹ Among other research, the Report discussed the study of the effects of irradiation on male reproductive function, funded by the Atomic Energy Commission; a study of potential addictive properties of untested analgesics on prisoners with history of drug addiction; and the experimental “treatment” of aggressive behavior with drugs, aversive conditioning techniques, and behavior modification through the deprivation of basic amenities.¹³² The Commission discussed the increased public sentiment against research on prisoners since the 1960s, as well as the Health Subcommittee of the Senate Committee on Labor and Public Welfare hearings in 1973 which cited exploitation and the impossibility of obtaining informed consent as reasons to prohibit research in prisons.¹³³ The Report went on to

¹²⁷ See 45 C.F.R. § 46.306.

¹²⁸ See Wener, *supra* note 40, at 371.

¹²⁹ See REPORT AND RECOMMENDATIONS, *supra* note 47.

¹³⁰ See *id.* at viii.

¹³¹ See *id.* at 1.

¹³² See *id.* at 1-2.

¹³³ See *id.* at 3.

highlight concern about abuses of psychosurgery and behavior modification programs in prisons, and cited the Director of the Federal Bureau of Prison's determination that participation by prisoners under federal jurisdiction in any medical experimentation should be phased out.¹³⁴

The Commission highlighted two main ethical dilemmas concerning the use of prisoners as clinical research subjects: "(1) whether prisoners bear a fair share of the burdens and receive a fair share of the benefits of research; and (2) whether prisoners are, in the words of the Nuremberg Code, 'so situated as to be able to exercise free power of choice' – that is, whether prisoners can give truly voluntary consent to participate in research."¹³⁵ Though this document predated the Belmont Report, the Commission alluded to the fundamental ethical principles which would later come to create the foundation of human subject research regulation. The Report noted that disproportionate use of prisoners in specific kinds of research would violate the principle of "justice," which requires that individuals and groups be treated fairly, and coercive prison environments may compromise the principle of "respect for persons" which requires the protection of individual autonomy.¹³⁶ The Report conceded that these issues were not undisputed, and upholding the principles of respect for persons and justice could in fact cut the other way. Respect for a person may require deference to his or her deliberate choice to volunteer for research, and systematic deprivation of the freedom to participate in clinical trials may violate the principle of justice, as it would deprive prisoners of benefits available to others.¹³⁷

However, the Commission stated its ultimate decision after weighing these competing principles, declaring, "When persons seem regularly to engage in activities which, were they

¹³⁴ *See id.* at 4.

¹³⁵ *See id.* at 5.

¹³⁶ *See id.* at 5-6.

¹³⁷ *See id.* at 6.

stronger or in better circumstances, they would avoid, respect dictates that they be protected against those forces that appear to compel their choices. It has become evident to the Commission that, although prisoners who participate in research affirm that they do so freely, the conditions of social and economic deprivation in which they live compromise their freedom. The Commission believes, therefore, that the appropriate expression of respect consists in protection from exploitation.”¹³⁸ With that, the vast majority of federally funded research on prisoners came to an end.

B. FDA Regulation of Research on Prisoners

Unlike HHS regulations which only apply to research institutions that receive federal funding, the FDA’s regulatory authority extends to any research pertaining to products under its jurisdiction.¹³⁹ While in many respects the FDA regulations closely resemble the Common Rule, including a similar Subpart D governing children as research subjects, conspicuously absent is any Subpart C or regulation of research on prisoners.¹⁴⁰ However, this was not always the case. In May of 1980, around the same time that HHS was promulgating its Common Rule, the FDA proposed a similar de facto ban on non-therapeutic, experimental research on prisoners.¹⁴¹ The FDA was seemingly convinced by the Commission’s finding of prisons as inherently coercive institutions and relied on the conclusion that researchers could never establish a compelling need

¹³⁸ *See id.* at 6-7.

¹³⁹ *See* 21 C.F.R. § 50.1. These products include food, dietary supplements that advertise a nutrient content or health claim, food and color additives, drugs and medical devices for human use, cosmetics, and biological products for human use. *Id.*

¹⁴⁰ *See* ETHICAL CONSIDERATIONS, *supra* note 121, at 88.

¹⁴¹ *See* 45 Fed. Reg. 36,386 (May 30, 1980), which was later codified at 21 C.F.R. §§ 50.1-.46. *See also* Schroeder, *supra* note 76, at 969. The rule permitted research on prisoners only if the research had the intent and reasonable probability of improving the health of the subjects, thereby banning nontherapeutic research. *Id.* at 969 n. 2.

to use prisoners as opposed to other research subjects.¹⁴² In addition to the requirement that any research on prisoners must be therapeutic, other criteria were enumerated: an institutional review board would have to find that “(1) living conditions in the prison were adequate so that prisoners were not being unduly influenced by the rewards of being research subjects; (2) nonprisoner volunteers would accept the same risks that the prisoners were being asked to accept; (3) procedures for the selection of the subjects were fair; (4) relevant information was provided in language understandable to the subjects; (5) prisoners’ participation would not be taken into account by parole boards; and (6) followup examination and care would be available and that subjects would be so informed.”¹⁴³ Following its proposal in the Federal Register, this ban on nontherapeutic research was to become effective on June 1, 1981.¹⁴⁴ However, this date was stayed after a lawsuit was filed challenging the regulation.¹⁴⁵

On July 29, 1980, four prisoners from the State Prison of Southern Michigan at Jackson filed a lawsuit in the United States District Court for the Eastern District of Michigan seeking a declaratory judgment invalidating the FDA proposed regulation and granting injunctive relief against its enforcement.¹⁴⁶ In November of that year, the Upjohn Company, which conducted the majority of its pharmaceutical research at the Jackson penitentiary, intervened as a plaintiff in the suit.¹⁴⁷ Claiming that the FDA’s proposed ban violated the equal protection and due process clauses of the Fifth Amendment, the plaintiffs alleged that:

¹⁴² See Schroeder, *supra* note 76, at 985.

¹⁴³ See *id.*; see also 45 Fed. Reg. 36,386, 36,391-92 (May 30, 1980).

¹⁴⁴ See 45 Fed. Reg. 36,386 (May 30, 1980).

¹⁴⁵ See 46 Fed. Reg. 18,951 (Mar. 27, 1981); see also 46 Fed. Reg. 35,085 (July 7, 1981).

¹⁴⁶ See Schroeder, *supra* note 76, at 986 (citing Plaintiff-intervenor Upjohn Company’s Complaint, *Fante v. Department of Health and Human Servs.*, No. 80-72778 (E.D. Mich. filed Oct. 10, 1980)).

¹⁴⁷ See *id.*

[t]he effect of the [FDA] proposal would be to eliminate clinical testing at Jackson and similar facilities, because most of the pharmaceutical studies at prisons involve ‘nontherapeutic’ research . . . [and] closing down such programs would deprive prisoners of their right freely to decide whether to participate in such programs, would deprive state correctional institutions of the rehabilitative and economic benefits for prisoners of such programs, and would injure the public by depriving pharmaceutical companies of the most suitable populations for certain kinds of studies¹⁴⁸

In response to the lawsuit, the FDA notified the public that the effective date of the regulation would be stayed until five months following the district court’s judgment on the merits of the suit.¹⁴⁹ On December 18, 1981, the FDA issued a reproposal of the rule noting the concerns expressed in the pending lawsuit and attempting to address those challenges with a reformulation of the regulation.¹⁵⁰ Unlike the earlier version of the regulation, the reproposal did not place an outright ban on nontherapeutic research.¹⁵¹ The FDA ultimately settled the case, explaining in the Federal Register that because only a small number of prisoners were actually used in nontherapeutic research, it was an inefficient use of agency time and resources to litigate the suit and uphold the validity of its proposed regulation.¹⁵² The notice in the Federal Register also explained that the agency was reconsidering its prior position based on “questions that have been raised concerning the need, utility, and costs” of the rule and planned to take another look at the proposed regulation, while indefinitely staying its implementation in the meantime without providing for public comment.¹⁵³ Following that notice, the indefinitely suspended regulations

¹⁴⁸ *See id.*

¹⁴⁹ *See* 46 Fed. Reg. 35,085 (July 7, 1981).

¹⁵⁰ *See* 46 Fed. Reg. 61,666 (Dec. 18, 1981).

¹⁵¹ *See id.*

¹⁵² *See* ETHICAL CONSIDERATIONS, *supra* note 121, at 88; *see also* 46 Fed. Reg. 35,085 (July 7, 1981).

¹⁵³ 46 Fed. Reg. 35,085 (July 7, 1981).

were ultimately removed from the Code of Federal Regulations and Subpart C of 21 C.F.R. Part 50 has remained “reserved.”¹⁵⁴

V. RECENT DEVELOPMENTS

A. 2006 IOM Report

The contrasting regulations of public and privately-funded nontherapeutic research on prisoners remained uncontested for nearly three decades until July of 2006. At that time, the Institute of Medicine released a report recommending that the government loosen its regulations on the use of prisoners as research subjects.¹⁵⁵ The publication of these recommendations invoked a wave of controversy and reintroduced the dispute over coercive prison environments into the public conversation. As one media outlet reported, “...it has dredged up a painful history of medical mistreatment and incited debate among prison rights advocates and researchers about whether prisoners can truly make uncoerced decisions, given the environment they live in.”¹⁵⁶ The shortage of potential research subjects available to the biomedical industry, coupled with fourfold increase in the prison population in the last 30 years—now consisting of approximately 2.3 million inmates—has created pressure to examine the reopening of prison gates to federally-funded medical researchers.¹⁵⁷ As explained in the report, “The charge of our Committee, the Institute of Medicine Committee on Ethical Considerations for Revisions to the DHHS Regulations for Protection of Prisoners Involved in Research, was to explore whether the conclusions reached in 1976 by the National Commission for the protection of Human Subjects

¹⁵⁴ See ETHICAL CONSIDERATIONS, *supra* note 121, at 88.

¹⁵⁵ See Urbina, *supra* note 23.

¹⁵⁶ *Id.*

¹⁵⁷ *Id.*

of Biomedical and Behavioral Research remain appropriate today.”¹⁵⁸ The Committee acknowledged that past abuse of research on prisoners “has engendered deep distrust among prisoners and their advocates” and that the prisoner population is comprised of a “disproportionate representation of . . . historically disenfranchised populations.”¹⁵⁹

However, the report countered that a total ban on prisoner research was a mistaken approach, noting that:

[r]esearch affords the potential of great benefit as well as burden. It can help policy makers to make correctional settings more humane and effective in achieving legitimate social goals such as deterrence and rehabilitation. Research can also help policy makers better understand and respond to the myriad health problems faced by prisoners such as HIV/AIDS, tuberculosis, hepatitis C, mental illness, and substance abuse. Respect for prisoners also requires recognition of their autonomy. If a prisoner wants to participate in research, his or her views should be taken into account. The overall goal, then, is to permit scientifically rigorous research to the extent that it confers significant benefit without undue risk and in accordance with the prisoner’s wishes.¹⁶⁰

In weighing these factors, the Committee found that the current federal regulation regime did not strike the proper balance between scientific advancement and prisoner protection.¹⁶¹ The “most glaring problem,” at the Report termed it, was that the federal rules covered only a small part of the research conducted in prisons—that which is funded by certain federal agencies covered by 45 C.F.R. Part 46.¹⁶² As such, one of the major changes that the Committee recommended was the implementation of universal standards of protection so that prisoner research safeguards would be implemented across the board regardless of the funding source of the research.¹⁶³ The other four main recommendations included: 1) expanding the definition of the term “prisoner” to

¹⁵⁸ ETHICAL CONSIDERATIONS, *supra* note 121, at ix.

¹⁵⁹ *Id.* at x.

¹⁶⁰ *Id.*

¹⁶¹ *See id.*

¹⁶² *Id.*

¹⁶³ *Id.*

include those on probation or parole; 2) shift from a category-based to a risk-benefit approach; 3) include collaborative responsibility into the ethical framework around this research; and 4) enhance the rigor of human subject protections with more stringent oversight.¹⁶⁴

B. 2011 Notice of Proposed Rulemaking

On July 22, 2011, the Department of Health and Human Services announced its intention to update the Common Rule in order to “ensure the highest standards of protections for human subjects involved in research, while enhancing effectiveness of oversight.”¹⁶⁵ In its press release announcing the Advance Notice of Proposed Rulemaking, HHS noted that the Common Rule has been in its current version since 1991 and that “an increase in multi-site studies have highlighted ambiguities in the current rules and have led to questions about whether the current regulatory framework is effectively keeping up with the needs of researchers and research subjects.”¹⁶⁶ The release went on to quote Harold Koh, HHS assistant secretary for Health, who remarked, “The adoption of the Common Rule two decades ago was a landmark event to ensure ethical practices and the safety of those individuals who participate in research. This regulatory review effort is primarily about enhancing protections for human subjects. The changes under consideration offer the promise of updating and enhancing those protections to keep pace with current challenges.”¹⁶⁷ The Advance Notice of Proposed Rulemaking in the Federal Register reiterates

¹⁶⁴ *Id.*

¹⁶⁵ Press Release, *HHS Announces Proposal to Improve Rules Protecting Human Research Subjects*, U.S. Department of Health and Human Services, July 22, 2011, available at <http://www.hhs.gov/news/press/2011pres/07/20110722a.html>.

¹⁶⁶ *Id.*

¹⁶⁷ *Id.*

this theme of hoping to find a contemporary balance between protecting human subjects while “facilitating valuable research and reducing burden, delay, and ambiguity for investigators.”¹⁶⁸

The Notice refers a few times to prisoners as a vulnerable population and the possibility for changes to Subpart C of the HHS Regulations. It also references changes that have been proposed by the Institute of Medicine which are being considered for adoption, and notes that public comment is being sought on these proposals. The agency acknowledges that, “The intent is to revise the Common Rule recognizing that other laws and regulations, such as the other subparts of the HHS human subjects protection regulations (Subparts B, C, and D, which deal with particular populations of vulnerable subjects...), FDA regulations, and the HIPAA Privacy Rule most likely will be affected and will need to be harmonized, as appropriate, with any proposed regulatory changes made to the Common Rule.”¹⁶⁹ The Notice also speaks at length to the goal of clarifying and harmonizing regulatory requirements and agency guidance, given the contradictory regulatory framework of the various agencies tasked with human subject research oversight.¹⁷⁰ Comments were solicited through September 26, 2011,¹⁷¹ but the public comment period was later extended upon request for one additional month through October 26, 2011.¹⁷² A brief review of a handful of these comments yields interesting results. For example, an MD/MPH from the Rollins School of Public Health at Emory University wrote to encourage reconsideration of the provisions for research on prisoners, citing the 2006 IOM report for its

¹⁶⁸ 76 Fed. Reg. 44,512 (July 26, 2011).

¹⁶⁹ *Id.* at 44,514.

¹⁷⁰ *Id.* at 44,528.

¹⁷¹ *Id.* at 44,512.

¹⁷² *See* 76 Fed. Reg. 54,408 (Sept. 1, 2011).

suggestions in improving oversight while opening the door to further research.¹⁷³ Another comment from a Ph.D. at East Carolina University emphasizes the need to universalize the Subparts of the Common Rule across agencies.¹⁷⁴ The comments submitted by researchers and medical doctors at the University of Rochester highlight the undue burden and inefficiency caused by the interpretation of Subpart C as including “incidental prisoners,” or research subjects who had already volunteered to participate in a trial and subsequently became incarcerated.¹⁷⁵ According to the comment, the mandated re-review of ongoing studies to identify this element is costly, time-consuming, and has no relation to the concerns about coercing prisoners to enroll in clinical trials while already imprisoned.¹⁷⁶

This ongoing discussion should yield results in the form of a new HHS rule regarding human subject research in the very near future. It remains to be seen whether the recommendations of the IOM will usher in major changes to the regulatory landscape of research on prisoners, and to what extent any changes made by HHS will affect the regulatory approach taken by the FDA.

VI. PROPOSALS FOR REGULATORY REFORM

The incongruity of federal regulations based on the funding stream for medical research had resulted in untenable loopholes and excessive barriers to scientific progress. The nearly

¹⁷³ Public Comment to *Human Subject Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators*, available at <http://www.regulations.gov/#!documentDetail;D=HHS-OPHS-2011-0005-0979>.

¹⁷⁴ Public Comment to *Human Subject Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators*, available at <http://www.regulations.gov/#!documentDetail;D=HHS-OPHS-2011-0005-1042>.

¹⁷⁵ Public Comment to *Human Subject Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators*, available at <http://www.regulations.gov/#!documentDetail;D=HHS-OPHS-2011-0005-1027>.

¹⁷⁶ *See id.*

wholesale ban on the use of inmates in clinical trials conducted by institutions or companies which receive federal funding is over-inclusive and excludes those prisoners who could give truly voluntary, informed consent from garnering the benefits of experimental treatment. Conversely, the relatively scarcity of oversight for private corporations using prisoners in clinical trials may result in unreported abuses and coercive arrangements which rob the prisoner of his or her autonomy. These divergent regulatory schemes should be brought into uniformity and universalized for all research involving prisoners as subjects.

Part C of the Common Rule promulgated by HHS includes important considerations for the composition of Institutional Review Boards when prisoners are involved in research.¹⁷⁷ Specifically, these regulations require that a majority of the Board have no association with the prison involved, and at least one member of the Board “shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity.”¹⁷⁸ The IRB must also ensure that any advantages accruing to participants are not of such a magnitude as

¹⁷⁷ See 45 C.F.R § 46.304.

¹⁷⁸ *Id.*; see also 45 C.F.R § 46.107(a). This regulation details the required composition of IRBs:

Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

compared to general “living conditions, medical care, quality of food, amenities, and opportunity for earnings in the prison” to constitute undue influence.¹⁷⁹ The Board is required to determine that the risks are commensurate with those that non-prisoner volunteers would agree to, that the information about the study is presented in understandable language, that parole boards will not take into account a prisoner’s participation and that the prisoner understands this fact, and that provisions have been made for appropriate follow-up examination or care if need be.¹⁸⁰

These guidelines and limitations take into account the risks of research in a potentially coercive environment. They are well-formulated and should remain in place. I would, however, suggest a few alterations. In terms of the composition of the IRB, having only one prisoner or prisoner representative may not be enough to adequately voice the concerns or preferences of prisoners as a class. The prisoner involved should have some experience with clinical research and should fully understand the risks and benefits of the trial. I am also not convinced that a prisoner representative can truly attest to the complexity of a lived experience inside of a prison, and thus would likely change this to require an actual prisoner or former prisoner to participate on the IRB. Another recommended change would involve the language with which the information about the risks and possible benefits of the research is communicated to the subject. Even if a consent form is written in clear, understandable language, studies report that approximately sixty to seventy-five percent of incarcerated adults are unable to read.¹⁸¹ Given the import of this staggering statistic, IRBs should ensure that prisoner subjects have an actual understanding of the possible risks involved in the clinical study as explained to them verbally,

¹⁷⁹ See 45 C.F.R. § 46.305(a)(2).

¹⁸⁰ See 45 C.F.R. § 46.305(a)(3)-(7).

¹⁸¹ Christopher Hensley, Richard Tewksbury, & Tammy Castle, *Characteristics of Prison Sexual Assault Targets in Male Oklahoma Correctional Facilities*, 18 J. INTERPERS. VIOLENCE 595, 604 (2003).

in their native language, rather than on a piece of paper which they may or may not have been able to read.

While these aspects of the Common Rule pertaining to prisoners are appropriate and necessary, the permitted research involving inmates is too restrictive and should be pared back. Limiting the use of prisoners to research particularly related to incarceration and criminal behavior effectively bans the use of prisoners in any clinical trial, even that which is therapeutic and could provide innovative treatment. As I have discussed above, the constitutional ramifications for banning seriously ill prisoners from experimental treatments signify that inmates should be permitted to participate under highly regulated and well-supervised conditions. These less restrictive alternative means should be employed rather than depriving both inmates and the medical community of mutually-beneficial opportunities for research.

The FDA should adopt the process-related HHS regulations, as well as some of the proposed changes raised by the Institute of Medicine's 2006 Report. These additional specific recommendations included the creation of a public database to track studies which involve prisoners and the inclusion in any clinical trial of non-prisoners as well as prison subjects to ensure that only reasonable risks are assumed by inmates.¹⁸² The Report also recommended the establishment of independent prison research advocates who will work on-site at the research ward and ensure that the clinicians on the ground continue to respect the autonomy of the prisoners throughout the research process.¹⁸³ Universalizing the regulatory landscape across all clinical trials on prisoners, regardless of the funding source, will ensure that prisoners will not be

¹⁸² *Should Prisoners Participate in Medical Research Trials?* PROTO-MASSACHUSETTS GENERAL HOSPITAL, available at <http://protomag.com/assets/should-prisoners-participate-in-medical-research-trials>.

¹⁸³ *See id.* at 2.

coerced or abused in the absence of federal oversight, but will also be permitted to access life-saving treatments through their informed consent to a federally-funded clinical trial.

CONCLUSION

The history of research on prisoners is a study in contradictions, with some prisoners during wartime earnestly seeking inclusion in clinical trials to give back to their country, while others were concurrently subjected to unspeakable abuse at the hands of medical researchers. Prisoners have filed lawsuits claiming constitutional violations for being forced into a clinical trial, while others have alleged in court that their constitutional rights were abridged by their preclusion from volunteering for research. The Department of Health and Human Services has placed an effective ban on all use of prisoners in clinical trials funded with federal dollars, while the Food and Drug Administration has very few guidelines or restrictions on the type of research or procedural precautions required for privately-funded research in prisons. It is unsurprising that opinions on this subject vary widely, and there has been ongoing debate for decades about the optimal solution to balance the interests of all parties involved. The FDA and HHS should harmonize their regulations in order to create a consistent scheme and to ensure that all prisoners are protected by a universal set of standards and guidelines. However, it is unjust for prisoners as a class to be denied the tangible benefits of clinical research, particularly when a well-trained IRB certifies that the experiment is beneficial and does not subject the inmates to any undue risk of harm. As two commentators aptly stated in reference to clinical trials of ground-breaking HIV drugs:

Inmates as a group . . . need to be provided with access to clinical trials of new and innovative therapies that present the possibility of direct benefit. . . . They must be presented with the opportunity for informed choice when appropriate, despite recognition that the systematic deprivations and inherent coerciveness of

the institutions and the desperate character of HIV infection compromise the consent process. As in other areas of public policy and public health, HIV infection demands a fresh examination of equity and justice. Whether access is provided to promising investigational therapies will measure the mettle, courage, inventiveness, and flexibility of the medical research community. It will also test the humanity of correctional administrators, who must provide the setting and support services to permit the conduct and monitoring of clinical trials.¹⁸⁴

This rousing call to innovation and compromise speaks to the need for policy makers and the medical community to reach a mutual understanding. It is imperative for the various interests touched by this debate to find a practicable solution that will serve the needs of prisoners and scientific progress while ensuring that that abuses of the past never again come to pass.

¹⁸⁴ Hoffman, *supra* note 24, at 515 (quoting Nancy Neveloff Dubler & Victor W. Sidel, *On Research on HIV Infection*, JOURNAL OF ACQUIRED IMMUNE DEFICIENCY SYNDROMES 174, 204 (1994)).